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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,735	04/29/2002	Andrew P. McMahon	21508-033	5366

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EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 06/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,735	MCMAHON ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *10-12 and 17-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9 and 13-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-20 are pending.

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-17 in Paper No. 9 is acknowledged. However, Applicants did not do the further election selected from the group consisting of Wnt-1, Wnt -3, Wnt -4, Wnt 7-a,Wnt-7b and a Wnt agonist HLDT86 as required by the previous Office Action.

2. During a telephone conversation with Attorney IngridA. Beattie on April 15, 2003, a provisional election was made Wnt-1 with traverse to prosecute the invention of group I, claims 1-17. Affirmation of this election must be made by applicant in replying to this Office action. Therefore, claims 10-12 and 17 along with other non-elected claims 18-20 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

3. Therefore, claims 1-9 and 13-16 in the scope of Wnt-1 polypeptide are considered.

4. Applicants are reminded to amend the claims 1-9 and 13-16 in the scope of Wnt-1 for reflecting the examination on the merits.

5. Applicants are reminded to cancel claims 10-12, 17 and 18-20 drawn to the non-elected groups.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-9 and 13-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for inducing a tubulogenesis of a renal metanephric messanchyme by co-culturing a metanephric messanchyme cells with another kind of cells that express wnt-1 polypeptide in an in vitro setting system, does not reasonably provide enablement for having a method of treating kidney disorder, renal failure, renal carcinoma, polycystic kidney

disease, chronic obstructive uropathy as well as a HIV-1 induced nephropathy by directly administering any or all Wnt protein except Wnt-11 into a mammal of an in vivo setting system. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

8. The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art would undue experimentation (See United States v. Theketronic Inc., 8USPQ2d 1217 (fed Cir. 1988). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. Theses factors were outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and gain in re Wands, 8USPQ2d 1400 (Fed. Cir. 1988). These factors include the following:

9. 1)& 2) State of art and unpredictability of the field.

10. The state of art teaches that a complete treatment of renal tissue damage is dependent upon a functional tissue that constitutes different kinds of cells and a fine orchestrated interaction between the meschyme and epithelium. The art teaches that a complex interaction of large number of biological factors responsible for growth, differentiation, pattern formation and morphogenesis of the renal tubule is required for the induction of renal cell growing and tubule development as taught by Humes t al. US patent No. 6,060,270A, see entire document, especially see section of background on col.1 and 2 and claims 1-6) and by Seppo V. (Trends in Glycoscience and Glycotechnology 1998, Vol. 10, pp. 335-347, see lines 15-24 on 1st col. of page 345).

11. Therefore, it is unpredictable that if only administering one Wnt-1 protein without other factors' coordination, a kidney tubule formation will occur in vivo.

12. Even Applicants own admit that Wnt protein may play an essential role in the initial tubulogenesis, but it need other cells coordinate since only supplying wnt-4 to the adjacent cells will induct the tubule formation in the spinal cord assay, indicating that other coordinating factors are required for the kidney cell tubulogenesis. Applicants also admit that Wnt protein may not be required for the late stage of morphogenesis of the tubule (See lines13-21 on page 38 of specification).

13. Another unpredictability is that Wnt-1 is a protooncogene. An aberrant activation of the Wnt/β-catenin signaling pathway by expressing Wnt-1 in an animal model is associated with numerous human cancers as evidenced by You et al. (J. Cell Biol. 2002, Vol. 157, No. 3, pp. 429-440, see abstract, Fig. 8 on page 436 and Fig. 9 on page 437) and Li et al. (Oncogen2, 2000, Vol. 19, pp. 1002-1009, see abstract).

14. Therefore, a result of an experimental inv vitro can not extrapolated into a result in an in vivo setting system.

15. The art at the time of application's invention was nil, with no demonstrative unambiguous successes in treating any renal regeneration in clinic with administering a Wnt polypeptide alone.

16. 3) & 4) Number of working examples and amount of guidance presented in the specification.

17. Specification only teaches that co-culture of isolated mesenchyme tissue with NIH3T3 cells expressing Wnt-1 induces a tubulogenesis (Table 5 on page 39) in an in vitro setting system.

18. However, specification does not teach a substantial purified Wnt-1 polypeptide can induce a regeneration of a damaged kidney tissue if it is administered into a mammal, wherein the animal is suffering from a kidney disorder, renal failure, renal carcinoma, polycystic kidney disease, chronic obstructive uropathy as well as a HIV-1 induced nephropathy in an in vivo setting system.

19. Applicants present no guidance on how the skilled artisan would practice successfully the treatment of renal problem as described supra in vivo.

20. 5) Scope of the claims. The claimed invention broadly read on to use a Wnt polypeptide for regenerating renal kidney tubule formation for a mammal suffering any or all kinds of kidney failure as recited in the claims 2-8.

21. 6) & 7) Nature of the invention and lever of the skill in the art.

22. The level of art of instant claimed invention involves one of the most complex and unpredictable fields of treating renal failure. The level of skill is required to practice the invention is very high at both medical and biotechnology fields.

23. Given the above analysis of the factors which the courts have determined are critical in asserting whether a claimed invention is enabled, it must be considered that the skilled artisan would have to conduct undue and excessive experimentation in order to practice the claimed invention.

Claim Rejections - 35 USC § 102

24. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

25. Claims 1 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Humes et al. (US patent No. 5,686,289A).

26. Claimed invention is interpreted as a method for stimulating kidney tubule in a post-natal mammal comprising administering a substitutive pure Wnt polypeptide 1 (claim 1) into an in vivo setting system (claim 16) for stimulating a renal tubule formation. Humes et al. teach a method for growing up renal tubule cells in ex vivo system comprises to culture kidney cells with a medium comprising a soluble factor selected from the group consisting of insulin like growth factor, Wnt-1 and Wnt-4 (Claims 1 and 5). Because growing kidney tubule cells is considered as a process of kidney tubule formation, and it is done by an ex vivo setting system, as claim 9 of instant application, especially Humes et al. also teach that the tubulogenesis is done with cells isolated from adult mammalian kidney and the experiment is not carried out in an embryonic, (See lines 29-30 on col. 15), it is considered that the procedure is done in a post-natal stage of a mammal. Therefore, the claimed invention is anticipated by the cited prior art.

Claim Rejections - 35 USC § 102

27. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who

has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

28. Claims 1 and 16 are rejected under 35 U.S.C. 102(e) as being anticipated by Humes et al. (US Patent No. 6,060,270A).

29. Humes teach an ex vivo method for growing renal tubule cells into a tubule-like structure with adult rabbit renal proximal tubule cells with a medium comprising Wnt-1 in combination with other components, such as TGF-β or α, retinoic acid, and EGF etc (See claims 1-6 and Exemplary Embodiments in col. 7-12). Because the claim invention does not limit that the claimed method is to use Wnt protein alone, the claimed invention is anticipated by the cited prior art.

30.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 703-305-1695. The examiner can normally be reached on 7:00 to 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Bao Qun Li June 29, 2003

Baoqun Li